Award Number:
 W81XWH-09-1-0722

TITLE:

High Risk Suicidal Behavior in Veterans- Assessment of Predictors and
Efficacy of Dialectical Behavioral Therapy

PRINCIPAL INVESTIGATOR:
 Marianne Goodman, M.D.

CONTRACTING ORGANIZATION: VA Medical Center
  Bronx, New York 10468

REPORT DATE: December 2015

TYPE OF REPORT: Addendum to Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
               Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT:

    X Approved for public release; distribution unlimited

The views, opinions and/or findings contained in this report are those of
the author(s) and should not be construed as an official Department of the
Army position, policy or decision unless so designated by other
documentation.

REPORT DOCUMENTATION PAGE

1. REPORT DATE (DD-MM-YYYY)	2. REPORT TYPE	3. DATES COVERED (From - To)
December 2015	Addendum to Final	29 Sep 2014 - 25 Sep 2015

4. TITLE AND SUBTITLE

High Risk Suicidal Behavior in Veterans- Assessment of Predictors and Efficacy of Dialectical Behavioral Therapy

5a. CONTRACT NUMBER
W81XWH-09-1-0722

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Marianne Goodman M.D.

Erin Hazlett, Ph.D.

email: marianne.goodman@va.gov

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

VA Medical Center
Bronx, New York 10468

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research
And Materiel Command
Fort Detrick, Maryland
21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Approximately one third of the Army's completed suicides last year occurred in the post-deployment period (Alvarez 2009) highlighting the importance of studying high-risk suicidal veteran populations. This project proposes two related studies. The first project is a randomized clinical trial of 120 veterans identified with high-risk suicidal behavior comparing the efficacy of Dialectical Behavioral Therapy (DBT) vs. treatment as usual (TAU) on suicidal behavior as a primary outcome measure. A second aim of the project is to examine group differences between 150 veterans at high risk (HR) for suicide and 150 veterans at low risk (LR) in a variety of symptom domains. The randomized clinical trial was completed with 93subjects. Results were notable for improvements in suicidality and secondary outcomes of depression, hopelessness and anxiety in both treatment groups, however there was not a significant difference between the treatment groups. DBT subjects did receive significantly more hours of treatment and for homeless, substance abusing males, there was considerable early drop-out in both arms. Our supplemental funding is to study affective startle as potential marker of suicide risk and as a marker of treatment outcome. Affective startle does significantly differ between Veteran ideators, single and multiple attempters. We collected additional female Veteran samples in a no-cost extension in order to perform gender sub-analyses.

15. SUBJECT TERMS
Borderline Personality Disorder, SUICIDE

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	UU	17	19b. TELEPHONE NUMBER (include area code)

Table of Contents

Introduction:

Approximately one third of the Army's completed suicides last year occurred in the post-deployment period (Alvarez 2009), highlighting the importance of studying high-risk suicidal veteran populations. This project proposes two related studies. The first project is a randomized clinical trial of 120 veterans identified with high-risk suicidal behavior comparing the efficacy of Dialectical Behavioral Therapy (DBT) vs. treatment as usual (TAU) on suicidal behavior as a primary outcome measure. A second aim of the project is to examine group differences between 150 veterans at high risk for suicide and 150 veterans at low risk in a variety of symptom domains. The goal of this will be to identify symptoms associated with suicidal behavior that may advise future treatment.

We will assess symptom domains including mood and substance use in our veteran population by comparing symptoms in low vs. high risk veterans recently discharged from the James J Peters VAMC (JJPVAMC) psychiatric inpatient unit. In addition, we will explore indices of interpersonal function and measure features that have some evidence of offering protection from suicide, which could be viewed as resilience factors. A particular emphasis of the present project is to characterize the nature of the interpersonal dysfunction in high risk individuals, as there exists very good evidence that social isolation, or a lack of a sense of "belonging" puts people at particularly high risk for suicide, in particular in a military sample . We intend to assess the impact of DBT vs. TAU on these symptom domains in addition to their impact on suicidal behavior.

Body:

In October 2011, a supplement to this project was approved to add a physiological measure, affective startle, to the baseline assessment and post- DBT treatment.

Aim 1 relates to a randomized clinical trial of Dialectical Behavior Therapy (DBT) vs. treatment as usual (TAU) in 120 veterans recently hospitalized with high-risk suicidal behavior. This will be accomplished under the leadership of Dr. Marianne Goodman, James J. Peters VAMC, Bronx, NY   10468

Aim 1: To examine, in a randomized controlled trial (RCT), the efficacy of a 6 month treatment with standard DBT (weekly individual sessions, skills training group and telephone coaching as needed) as compared to TAU in 120 veterans recently discharged from an acute psychiatric inpatient stay with high risk suicidal behavior. The primary treatment outcome will be a quantification of suicidal events, as assessed by the Columbia Suicide Severity Rating Scale, which measures suicide attempts, plans and preparations. Our study will be powered to examine treatment assignment differences in this measure. Secondary outcomes will include suicidal ideation, parasuicidal events, treatment compliance, depressed mood, substance abuse and hopelessness.

This aim involves recruiting 120 veterans off the JJPVA "high-risk" suicide list; a designation made primarily after psychiatric inpatient admission for serious suicidal behavioral. High-risk (HR) suicide subjects will undergo a comprehensive diagnostic interview prior to entering the treatment study. Subjects will receive 6 months of TAU vs. DBT but both groups will continue to receive standard psychopharmacology and case management services from their clinic providers. Subjects will receive a battery of assessments at month 6, 12 and 18.

Aim 2 relates to a comparison of high-risk and low-risk suicidal veterans in interpersonal functioning and resilience, in an effort to identify intermediate symptoms that are closely associated with HR suicidal behavior. This will be accomplished under the leadership of Dr. Marianne Goodman, James J. Peters VAMC, Bronx NY   10468

Aim 2: To recruit veterans recently discharged from an acute psychiatric inpatient stay comparing 150 veterans with HR suicidal behavior to 150 veterans without such behavior (LR) in symptom domains focusing on interpersonal functioning and resiliency.

Aim 3 is exploratory and examines the effect of treatment (DBT or TAU) on the putative intermediate symptom domains associated with HR suicidal behavior of interpersonal functioning and resiliency. This will be accomplished under the leadership of Dr. Marianne Goodman James J. Peters VAMC, Bronx NY   10468

Aim 3: To explore the effect of DBT on the candidate intermediate symptoms of interpersonal functioning and resiliency associated with HR suicidal behavior.

<u>**Promised work:**</u>
<u>**Parent Project-**</u>
The first 3 months is devoted to training the raters on our assessment and diagnostic battery while we await regulatory approvals. During months 3-6, we expect to perform thirty baseline assessments and 15 high-risk subjects will be randomized to treatment. During months 6-12, 12-18, 18-24, 24-30, we expect that thirty high-risk and thirty low-risk suicidal subjects will receive baseline assessments during each 6 month block. We anticipate that 25 of the high-risk subjects will proceed into treatment during each one of the time blocks. Months 30-36 will target 30 total additional assessments for baseline high and low-risk subjects with 5 of the HR individuals being randomized for treatment. The baseline assessment is a more comprehensive evaluation and we estimate that it will take approximately 6-7 hours with follow-up assessments requiring 1-2 hours.

While we met recruitment goals for Aim 1 of the study, our recruitment for the RTC fell behind. In order to continue recruitment we requested and were granted a fifth year, no cost extension.
The Table below reflects promised work, and new numbers with the 5th year added.

	Baseline assessments (50% HR, 50% LR)	Randomized to treatment (HR only)	Follow-up assessments 6mo 12 mo 18mo		
Months 0-3	-----	-----	-----	-----	-----
Months 4-6	30	15	-----	-----	-----
Months 7-12	60	25	12	-----	-----
Months 13-18	60	25	19	11	-----
Months 19-24	60	25	19	17	10
Months 25-30	60	25	19	17	15
Months 31-36	30 –	5 –	19	17	15
Months 37-48 (year 4)	**New year 4 target- 60** Actual 65 293 to date (goal 300)	**New year 4 target-25** Actual 15 90 to date (goal 120)	28	19	30
Months 49-60 (year 5)	**New year 5 target- 10** Recruitment just to meet RTC goals	**New year 5 target-10** 15	15	20	30

<u>**Progress Parent Study:**</u>

IRB approval

Towards accomplishing these aims, we received approval from our local IRB 7/9/09 and local Research and Development approval on 7/15/2009; prior to official funding of the project. This allowed us to *pilot* the intervention, assessments and randomization procedure. Dept of Defense approval was obtained on 4/27/2010; almost four months later that we had projected in our initial statement of work.

Recruitment

No-cost extension year: During our no-cost extension year, we focused solely on increasing our female Veteran subject pool in order to be able to do gender analyses. In addition, we realized that our LR pool of female veterans needed to be augmented. During this time period, we recruited and successfully assessed an additional **11** females who completed our baseline assessment and affective startle paradigm

For the treatment trial, during our no cost extension year, we completed follow-ups.

Over the entire course of the study, **384** veterans have signed consent (248 high-risk subjects and 136 low-risk subjects) and **340** (221 high-risk and 119 low-risk) have completed baseline assessments. With these numbers, we have *surpassed our goal of 300 completed assessments*. However, recruitment for the treatment trial remained limited and we randomized a total of 93 subjects to the trial and 53 completed the 6-month treatment.

Summary of Entire Parent Study to date

	High Risk	*Low Risk*
# consented	248	136
# completed	221	119
# randomized	93	--
#complete 6 month	53	--
12 month f/up	49	--
18 month f/up	43	--

Randomized Treatment Trial:
Over the course of the project- **93** subjects have been randomized (to 45 TAU/48 to DBT).
53 subjects have completed the 6-month treatment trial; 25 for DBT and 28 for TAU.

Longitudinal Follow-up at 12 and 18 months:
49 subjects have completed 12-month follow up to date including- 22 DBT subjects and 27 TAU subjects and **43** subjects have completed the entire study (e.g. 18-month completers) including 19 DBT and 24 TAU subject.

Total: **340** of 300 completed baseline assessments (exceeded goals)
      93 of 120 randomized to clinical trial

Progress Pertaining to Aim #1
    Our Statement of work projected that by study completion we will have 300 baseline assessments finished. We completed 340, and during our no-cost extension year targeted females in order to perform gender sub-analyses. Data analysis was the focus of our no-cost extension year and we generated several manuscripts. Interim analyses have yielded findings pertaining to the importance of Axis I diagnoses of substance abuse, Axis II diagnoses of borderline personality disorder and responses on the interpersonal psychological survey as important risk factors for identifying "high-risk" veterans (see **Figure 1**)**.**

The identification of the interpersonal psychological survey as a critical instrument has led us to further examine its contents through a computerized implicit task assessment that we will be piloting in year 5 (see **Figure 2**).
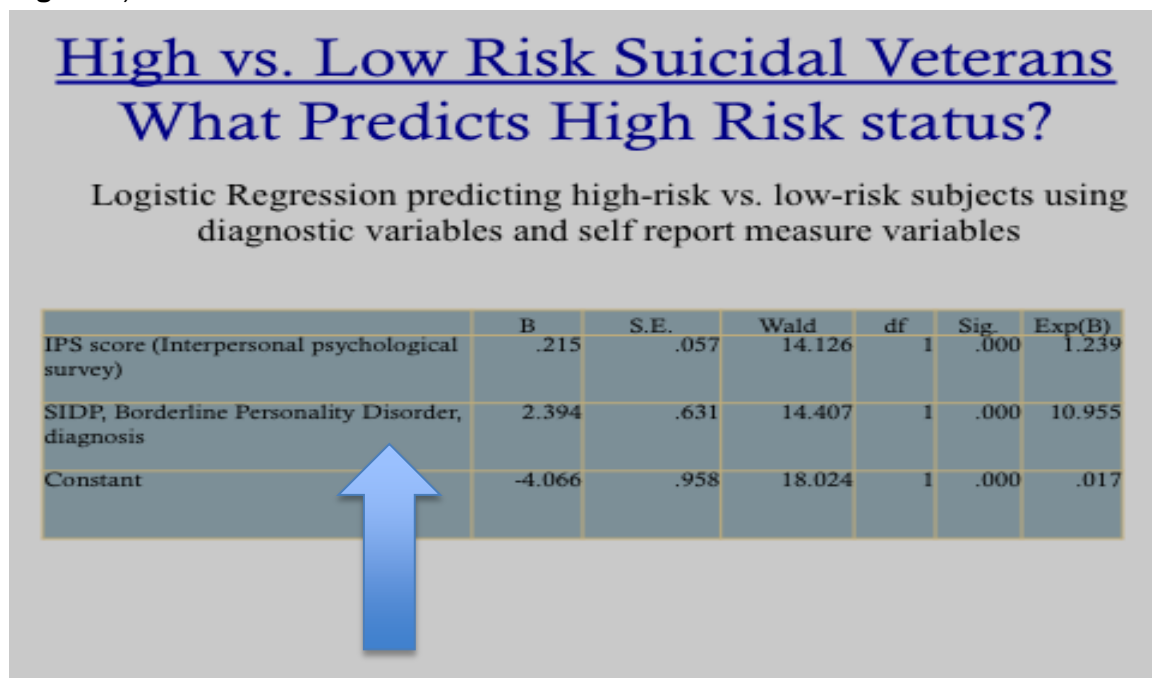

High vs. Low Risk Suicidal Veterans
What Predicts High Risk status?

Logistic Regression predicting high-risk vs. low-risk subjects using diagnostic variables and self report measure variables

	B	S.E.	Wald	df	Sig.	Exp(B)
IPS score (Interpersonal psychological survey)	.215	.057	14.126	1	.000	1.239
SIDP, Borderline Personality Disorder, diagnosis	2.394	.631	14.407	1	.000	10.955
Constant	-4.066	.958	18.024	1	.000	.017

Figure 1- Predictors of Suicide Risk in Veterans

Interpersonal Psychological Survey

Thwarted Belongingness
• I am alone

Lethal Suicide Attempts

Capacity for Suicide

Perceived Burdensome-ness
• I am a burden

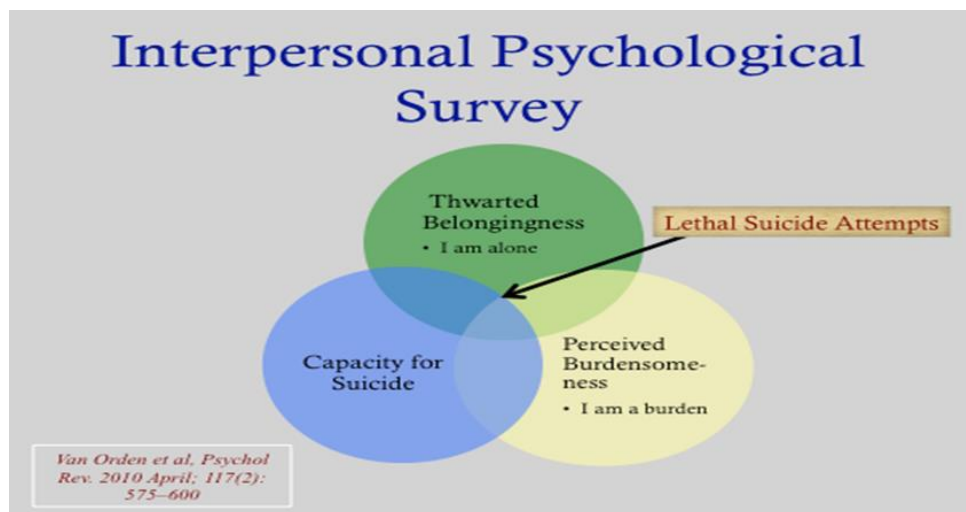Van Orden et al, Psychol Rev. 2010 April; 117(2): 575–600

Figure 2- Interpersonal Psychological Survey components

Progress Pertaining to Aim #2
We have randomized 93 subjects to the treatment trial and completed data analyses. Results are pictured below. Our findings indicate that both dialectical behavior therapy (DBT) and enhanced treatment as usual (TAU) were beneficial to suicidal Veterans, but there *were no significant differences between treatment groups in our primary or secondary outcome measure*s (see **Aim 2 Figures 1-5**). DBT utilized considerably more treatment sessions (see **Aim 2-Figure B**). Survival Curves for suicide ideation and re-hospitalization also showed no differences (see **Aim 2 Figures 6-7**). These results were accepted for publication, citation below:
Goodman, M., Banthin, D., Blair, N., Mascitelli, K.A., Wilsnack, J., Chen, J.,
Messenger, J., Perez-Rodriguez, M., Triebwasser, J., Koenigsberg, H.W., Goetz,
R., Hazlett, E.A., New, A.S. A Randomized Trial of Dialectical Behavior Therapy in
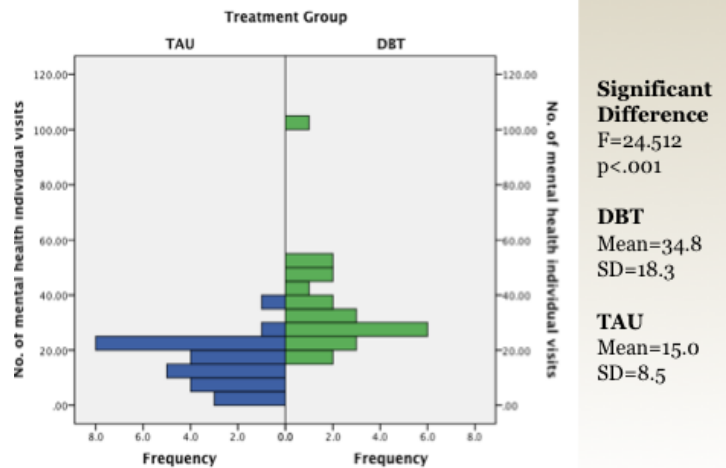High Risk Suicidal Veterans. *J Clinical Psych, in press.*

Weeks in TAU
28 Completed

Weeks in DBT
### 25 Completed
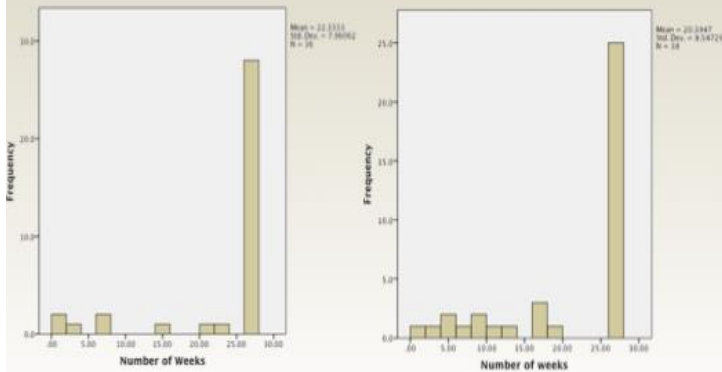
Aim 2- Figure A: # weeks in Treatment

Mental Health Individual Visits

Significant Difference
F=24.512
p<.001

DBT
Mean=34.8
SD=18.3

TAU
Mean=15.0
SD=8.5

Aim 2- Figure B: # Mental Health Visits by Treatment Group

Figure 1.) Comparison of C-SSRS Ideation Ratings among veterans at high risk for suicide, receiving either Treatment As Usual (TAU) or adjunct Dialectic Behavior Therapy (DBT).
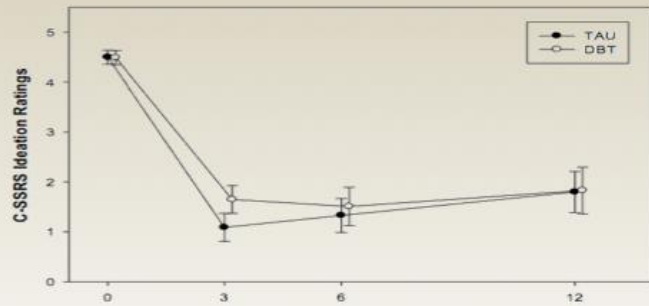
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	177.723	13.157	.000
TXGRP	1	120.598	.696	.406
VISIT	3	76.995	103.199	.000
AGE	1	164.978	.767	.382
SEX	1	151.432	.157	.693
EDUC	1	163.431	2.117	.148
TXGRP * VISIT	3	77.273	.543	.655

Aim 2- Figures 1-5:
Primary Outcome Measures by Treatment Group-
Figure **1**- Suicide Symptomatology (measured by the CSSRS)
Figure **2**- Suicide Ideation (measured by the Beck Suicide Ideation scale)

Secondary Outcome Measures by Treatment Group-
Figure **3**- Depression (measured by the Beck Depression Scale)
Figure **4**- Hopelessness (measured by the Beck Hopelessness Scale)
Figure **5**- Anxiety (measured by the Beck Anxiety Scale)

** Note improvements across time in both treatments, however no significant difference between treatment groups

Figure 2.) Comparison of Beck Suicide Scale Ratings among veterans at high risk for suicide, receiving either Treatment As Usual (TAU) or adjunct Dialectic Behavior Therapy (DBT).
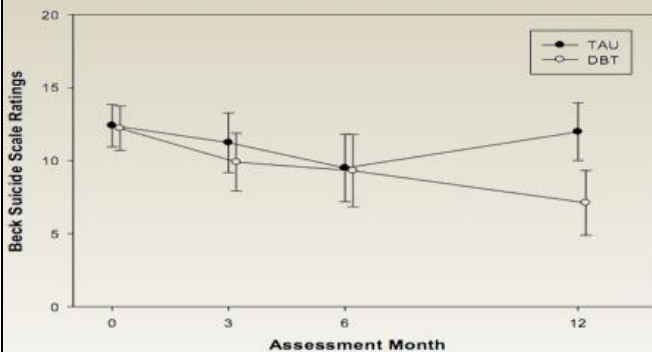
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	80.496	.191	.664
TXGRP	1	92.896	.673	.414
VISIT	3	119.101	1.576	.199
AGE	1	83.944	1.232	.270
SEX	1	92.020	1.036	.312
EDUC	1	82.442	3.256	.075
TXGRP * VISIT	3	119.379	.890	.448

Figure 3.) Comparison of Beck Depression Inventory among veterans at high risk for suicide, receiving either Treatment As Usual (TAU) or adjunct Dialectic Behavior Therapy (DBT).
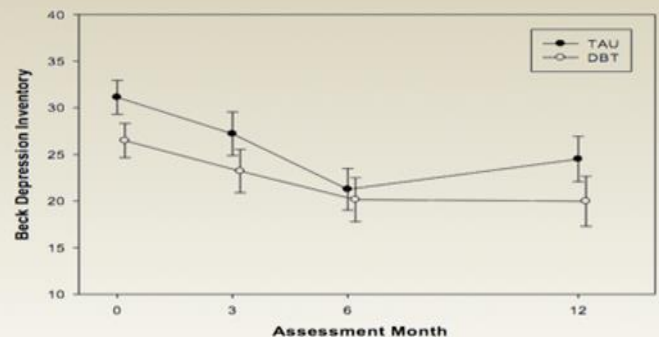
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	89.101	2.267	.136
TXGRP	1	92.459	2.465	.120
VISIT	3	157.464	8.768	.000
AGE	1	86.055	4.877	.030
SEX	1	95.202	1.209	.274
EDUC	1	88.364	.086	.770
TXGRP * VISIT	3	157.431	.432	.730

8

Figure 4.) Comparison of Beck Hopelessness Scale Ratings among veterans at high risk for suicide, receiving either Treatment As Usual (TAU) or adjunct Dialectic Behavior Therapy (DBT).
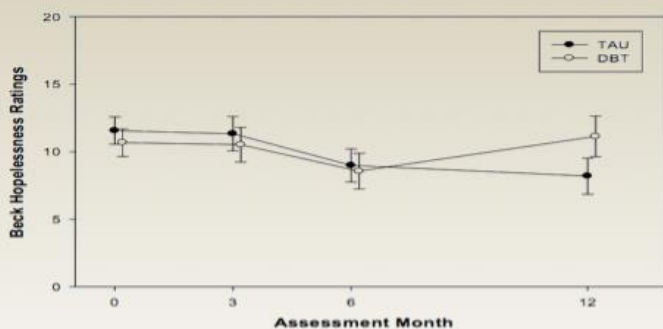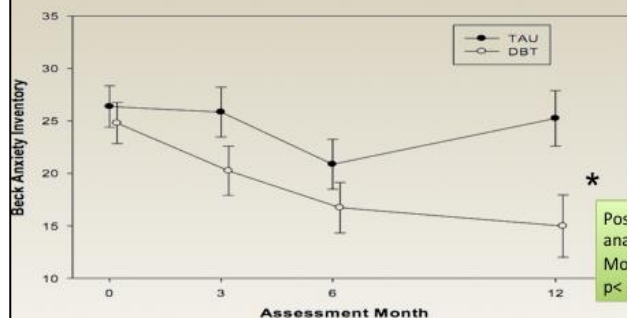

Type III Tests of Fixed Effects				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	83.909	3.230	.076
TXGRP	1	89.018	.023	.879
VISIT	3	149.339	2.775	.043
AGE	1	81.911	4.938	.029
SEX	1	90.369	.049	.825
EDUC	1	83.408	.305	.582
TXGRP * VISIT	3	149.104	1.423	.238

Figure 5.) Comparison of Beck Anxiety Ratings among veterans at high risk for suicide, receiving either Treatment As Usual (TAU) or adjunct Dialectic Behavior Therapy (DBT).
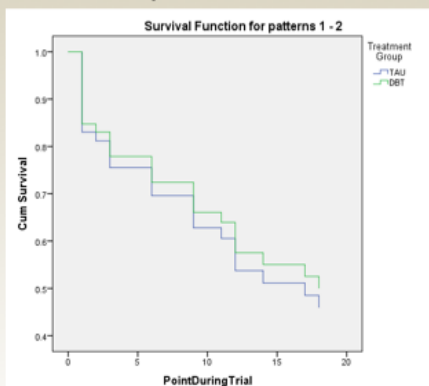

*

Post-hoc analysis: Month 12 BAI p< .021

Type III Tests of Fixed Effects				
Source	Numerator df	Denominator df	F	Sig.
Intercept	1	84.869	4.475	.037
TXGRP	1	90.271	4.666	.033
VISIT	3	144.281	4.718	.004
AGE	1	85.340	1.125	.292
SEX	1	91.790	.173	.679
EDUC	1	86.065	.061	.805
TXGRP * VISIT	3	144.255	1.761	.157

Survival Analysis: Suicidal Ideation

DBT 50% w/o ideation @ 18 months
TAU 46% w/o ideation @ 18 months
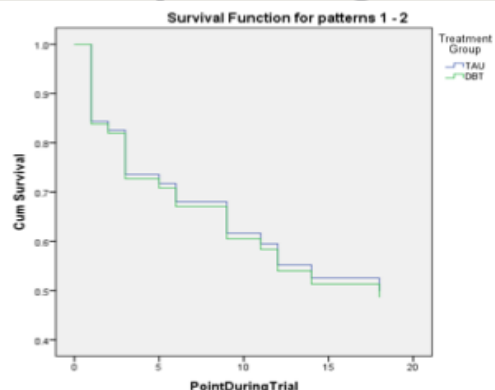
ADDITIONAL ANALYSIS- SURVIVAL ANALYSES
Aim 2- FIGURES 6 and 7:
Survival Analysis – Suicide Ideation
Survival Analysis- Re-Hospitalizations
** Note almost identical survival curves between the two treatment groups. Note very high rate of re-hospitalization.

Survival Analysis: Hospitalizations

Both treatment groups @ about 51% w/o hospitalizations.

Progress Pertaining to Aim #3
There were no significant differences found between treatment groups in the domains of interpersonal functioning nor resiliency.

Problems Accomplishing Tasks

With Hurricane Sandy, the Manhattan VA hospital was closed for upwards of 5 months. This lead to disruptions of care at our facility, as Manhattan patients sought treatment temporarily at our hospital. This complicated RCT recruitment efforts as pts were less likely to enroll in a longitudinal study that would require changing the location of their outpatient care beyond the expected time of Manhattan VA's closure.

SUPPLEMENT:

In addition to our three aims for the parent study, we added three additional aims for the supplemental study:

Supplement Aim 1 is to conduct a nonverbal and objective psychophysiological assessment of emotion processing using the affective startle paradigm to test whether it might serve as a potential biomarker for differentiating levels of suicidality. This will be accomplished under the leadership of Drs. Marianne Goodman and Erin Hazlett, James J. Peters VAMC, Bronx NY   10468

Aim 1. To examine the magnitude, time course, and rate of habituation of the startle eyeblink response during unpleasant, neutral, and pleasant pictures in 150 veterans with varying levels of suicidality; 60 veterans with a recent suicide attempt (during past 3 months), 60 veterans with suicidal ideation but no history of attempts, and 30 healthy veteran controls (i.e. no current psychiatric diagnosis).

This aim will be accomplished by adding the affective startle modulation paradigm to our current assessment battery of high- and low-risk suicidal subjects. Eligible subjects enrolled in the DoD funded parent project will participate in a 1-hour psychophysiology session at the MIRECC psychophysiology laboratory where we will record our primary variable of interest, namely the affective startle eyeblink response at baseline and 6 months for those enrolled in the DoD treatment trial. During this session, participants will view an intermixed series of unpleasant, neutral, and pleasant pictures from a standardized picture set. For each of the 3 picture conditions, we will examine three measures related to affective startle eyeblink modulation which is our psychophysiological measure of emotion processing: (1) the *amplitude* of the startle eyeblink response; (2) the *time course* of emotion processing by presenting the startle probes at different times during and post-picture processing; and (3) the rate of *habituation* of the startle eyeblink response.

Supplement Aim 2 is to compare startle variables across suicide groups (ideators, attempters) by presence or absence of borderline personality disorder to clarify if differences in affective startle modulation extend beyond personality disorder diagnosis. Thirty suicide attempters with BPD (SABPD+) will be compared with 30 suicide attempters without BPD (SABPD-) and 30 suicide ideators with BPD (SIBPD+) will be compared to 30 ideators without BPD (SIBPD-) across startle variables. This will be accomplished under the leadership of Drs. Marianne Goodman and Erin Hazlett, James J. Peters VAMC, Bronx NY   10468

Aim 2 investigates the relationship of Axis II diagnosis, suicidality and affective startle. The collected data for Aim 2 will be used to explore this question.

Supplement Aim 3 (No-Cost Extension) is to explore gender differences between male and female veterans regarding affective startle modulation and using lifetime number of suicide attempts as a continuous variable of interest. Fifty female veterans will be compared with fifty male veterans for this analysis. This will be accomplished under the leadership of Drs. Marianne Goodman and Erin Hazlett, James J. Peters VAMC, Bronx NY   10468

Aim 3 investigates the relationship of gender, suicidality and affective startle. We will investigate potential differences in affective startle response across gender and suicide status.

<u>**Supplement Promised Work:**</u>

	Supplement: Startle assessments:			
	Pt Baseline	Pt 6mo	HC Baseline	HC 6mo
Months 13-18	Obtain IRB approval			
Months 19-24	45	-----	12	----
Months 25-30	50	23 *	12	10
Months 31-36	25	22 *	6	11
Months 37-42	----	5 *	----	4
Months 43-48				

The project was awarded funding on 9/24/2011. In its first 12 months, the research team was incredibly effective in mobilizing resources and enrolling and testing **94** subjects at baseline and completing **1** 6-month follow-up. Over the next 12-month period (10/1/12 → 9/30/13), the team was similarly effective with recruitment, testing an additional **55** subjects at baseline and **13** at 6-months following the treatment trial. In the 12-month period (10/1/13 → 9/30/14), we have tested additional **21** subjects at baseline and **9** at 6-months. The vast majority of these new participants were female (18/19), as we redoubled efforts to recruit from this population at the JJPVAMC. During the no-cost extension year, we added **6** additional females. These figures bring the cumulative total of baseline and 6-month numbers to **177** subjects and **23** subjects respectively.

<u>Progress Pertaining to Supplement Aim #1</u>

Since receiving funding, we have run **177** patients at baseline, **exceeding our goals**, and have done **23** 6-month follow-ups and therefore have met our recruitment goals for supplement Aim #1. The overall breakdowns are as follows:

Group	Recruitment - Total
Controls	**38** (9F/29M)
Ideators	**46** (14F/32M)
Single Attemptors	**44** (14F/30M)
Multiple Attemptors	**49*** (23F/26M)
6-Month Follow-Up	**23** (6F/17M)

*Four patients reclassified as a Single Attemptors

<u>Preliminary analyses</u> on the first **108** subjects demonstrated a significant interaction between affective startle and suicide risk. (see **Supplement figure 1**). Multiple ideators, in the unpleasant picture condition, had significantly elevated affective startle % change values as compare to single attempters and ideators (both active and passive).

Group x Picture Type interaction, F[6,206]=2.92, p<0.01
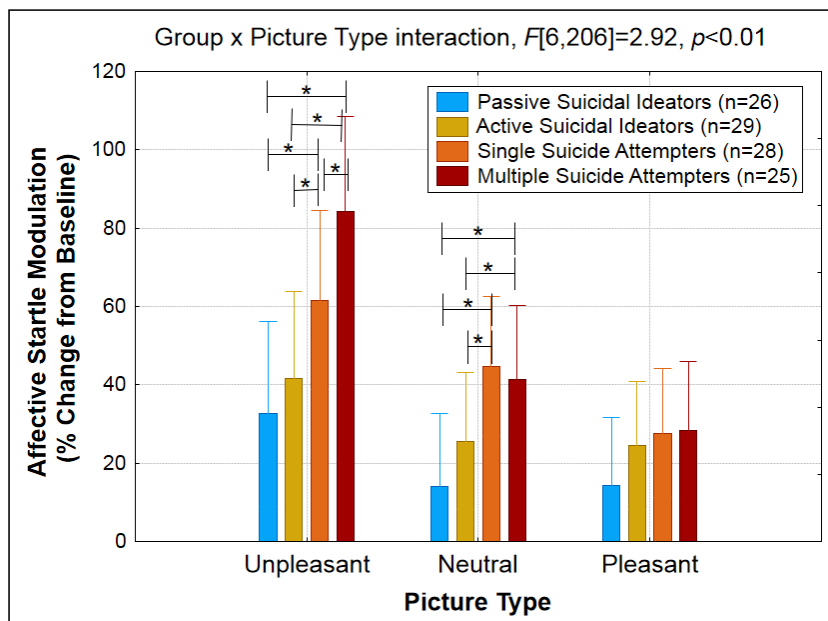
Supplement/Figure 1.
Affective Startle and Suicide Risk in veterans with passive ideation, active ideation, and a history of single and multiple suicide attempts (preliminary data, n=108).

Demographic & Baseline Data

	Non-attempters (ideators)	Attempters	
Number	56	70	All subjects recruited from Parent DoD Study- Predictors of High Risk Suicide and Efficacy of DBT
Age	37.7±9.4	41±11.4	
Females	19	28	
Males	37	42	
Unemployed / Student	85%	79%	
Last Suicide attempt (months prior)	0	75±80.1	
CSRSS- Ideation	2.0±1.0 (n=56)	4.6±0.7 (n=70)*	
Beck Depression	17.47 ± 14.34 (n=56)	26.5 ±11.9(n=70)*	
Beck Anxiety	16.3 +/- 13.8 (N=54)	22.5 +/- 11.5 (N=62)*	
DERS Total	87± 30.2 (n=55)	105.2 ±24.9 (n=68)*	
DIB-R score	4.6 ± 2.8 (n=56)	7.2 ± 2.3(n=70)*	
Combat Exposure Scale	5.8± 8.2 (n=55)	7.3±9.1 (n=69)	

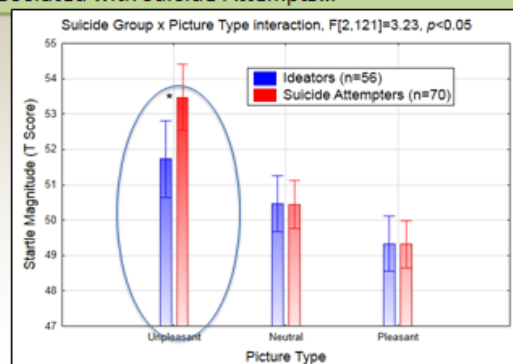* Non-attempters vs. Attempters p<0.01

Supplement Figure 2.
The data was also analyzed by collapsing suicide groups to ideators vs. attempters. Using a larger data set of 126 of the Veterans, attempters demonstrated significantly greater levels of depression, anxiety, borderline PD symptoms and emotion dysregulation scores (see demographic slide).

Supplement Figure 3.
Affective startle in attempters vs. ideators
Startle amplitude to emotional pictures in suicide attempters was significantly different from ideators in the unpleasant picture condition only.

Startle Amplitude by Picture Type in Attempters vs. Non-attempters (n=126)

Greater startle amplitude during unpleasant pictures is associated with Suicide Attempts...

Suicide Group x Picture Type interaction, F[2,121]=3.23, p<0.05

12
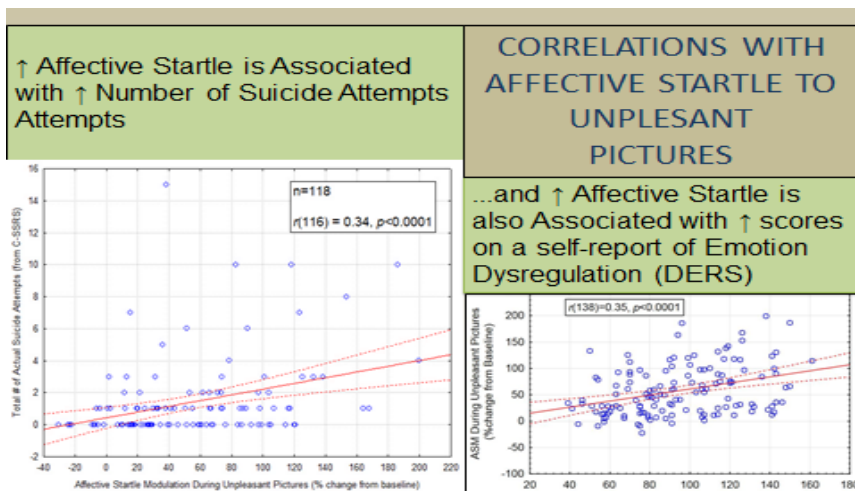
Supplement Figure 4. Correlations with Affective Startle. This figure shows that the affective startle finding of increased amplitude to unpleasant pictures collapsed across all subjects correlates with the number of suicide attempts and increased scores of the difficulty of emotion regulation scale.
These findings suggest that affective startle may be a biomarker of suicide risk.

In addition, using data from the treatment trial participants who received affect startle, amplitude to unpleasant pictures was used prospectively to examine prospective suicide attempt risk. Increased amplitude to unpleasant pictures was significantly associated with prospective suicide attempt** in a small sample of treatment participants.

Progress Pertaining to Supplement Aim # 2
See information pertaining to Aim #1, specifically figure #4 above.

Progress Pertaining to Supplement Aim # 3 (NCE)
A newly added Aim for our approved No-Cost Extension was to continue to gather data from female participants. Female sub-analyses are still being conducted.

Problems Accomplishing Tasks
We did not experience any difficulty recruiting for this project and are in fact were ahead of schedule.

Key Research Accomplishments for both Parent and Supplement Projects

We have just completed year 5 of the parent study and no-cost extension for the affective startle supplement.

- Since DoD IRB approval (4/27/10): parent subject recruitment has been brisk. **384** Veteran subjects have signed consent.
- **340** (out of promised 300) subjects completed baseline assessments.
- **93** HR patients were randomized to the treatment trial,
- **53** HR patients have completed the 6-month treatment trial,
- **177** subjects have completed baseline affective startle
- **Treatment trial results suggest that DBT is no more effective than enhanced treatment as usual for suicidal Veterans.**
  - ****** however both groups had significant drop out rates and difficulty with engagement.

Future directions for research suggest alternative modalities for early engagement post hospitalization.

- Affective startle is a potential biomarker of suicide risk.
- Preliminary data shows affective startle may predict prospective suicide attempts.

Reportable Outcomes

Publications

Treatment trial results:
Goodman, M., Banthin, D., Blair, N., Mascitelli, K.A., Wilsnack, J., Chen, J., Messenger, J., Perez-Rodriguez, M., Triebwasser, J., Koenigsberg, H.W., Goetz, R., Hazlett, E.A., New, A.S. A Randomized Trial of Dialectical Behavior Therapy in High Risk Suicidal Veterans. *J Clinical Psych, in press.*

Data from the baseline study:
Kayman, D. J., Goldstein, M. F., Dixon, L., Goodman, M. (2015). Perspectives of Suicidal Veterans on Safety Planning: Findings From a Pilot Study. *Crisis: The Journal of Crisis Intervention and Suicide Prevention 36*(5): 371-383, doi: 10.1027/0227-5910/a000348.

Data from the supplement study:
Hazlett E, Blair N, Maxcitelli K, Perez-Rodriqiez M, New A, Goetz R, Goodman M.
Startle Amplitude During Unpleasant Pictures is Greater in Veterans with Multiple-Suicide Attempts and Predicts Future Suicide Attempt. *Psychophysiology*, under review.

Dissemination/Presentations
1) American Psychiatric Association, May 2012
2) DOD/VA Joint Conference Suicide Prevention, June 2012
3) Society Psychophysiology, Research, September 2012*, Sept 2014*,
4) Veterans Integrated Service Network (VISN) 3 Conference on
Addressing Mental Health Needs of OEF/OIF Soldiers, October 2012
5) American Psychiatric Association, May 2013
6) North American Society for Personality Disorders (NASSPD), April
2013* (2 presentations), 2015

Posters
1) International Society of Psychoneuroendocrinology (ISPNE) special
meeting on Biomarkers of PTSD, September 2012*
2) NASSPD, April 2013, April 2014, March 2015*
3) Biological Psychiatry May 2013*, May 2014*
4) International Society Psychophysiology, September 2013*

- **DoD supplement**

Conclusion:

Our preliminary baseline data highlights the importance of Axis II psychopathology, in particular, borderline personality disorder as a risk factor for high-risk suicidal behavior. This is relevant as the disorder is often

under recognized in VA settings and not even listed in the Uniform Services Package, the document listing required services for Veterans.

Enhanced Treatment as Usual and DBT are both effective treatments for suicidal veterans, however there is no significant difference between treatments and DBT results in enhanced treatment delivery needs. Future directions for research should be targeted to better engagement of high risk suicidal veterans, who do not follow up with outpatient psychotherapy treatments as both groups had high drops out in this subset. These individuals were primarily male, homeless and abusing substances.

Regarding our supplemental funding for affective startle, a psychophysiological assessment tool, there does appear to be a significant relationship between the affective startle response to negative picture probes and number of suicide attempts. These results suggest that the processing of negative emotion is a critical element of suicide attempt history. Future studies using affective startle include whether this measure can predict those at suicide risk prospectively. We are currently piloting a portable version of the affective startle assessment which will allow us to assess individuals in different setting (e.g. emergency room, inpatient unit, off campus locations).
We continue to analyze our data for gender differences.

References:

Alvarez, V (2009). Suicides of Soldiers Reach High of Nearly 3 Decades <u>New York Timescom</u>. New York, New York Times.

Appendices: none included

Supporting Data: none included

Affective Startle Modulation in Suicidal Veterans

DMRDP Proposal Number WX81XWH-09-1-0722

PI: Goodman, Marianne   **Org:** James J. Peters VAMC, Bronx NY   10468   **Award Amount: $452,834**

DMRDP

Study/Product Aim(s)

Aim 1 is to examine the magnitude, time course, and rate of habituation of the startle eye blink response during unpleasant, neutral, and pleasant pictures in 150 veterans with varying levels of suicidality; 60 veterans with a recent suicide attempt (during past 3 months), 60 veterans with suicidal ideation but no history of attempts, and 30 healthy controls

Aim 2 is to compare startle variables across suicide groups (ideators, attempters) by presence or absence of borderline personality disorder to clarify if differences in affective startle modulation extend beyond personality disorder diagnosis. Thirty suicide attempters with BPD (SABPD+) will be compared with 30 suicide attempters without BPD (SABPD-) and 30 suicide ideators with BPD (SIBPD+) will be compared to 30 ideators without BPD (SIBPD-) across startle variables.
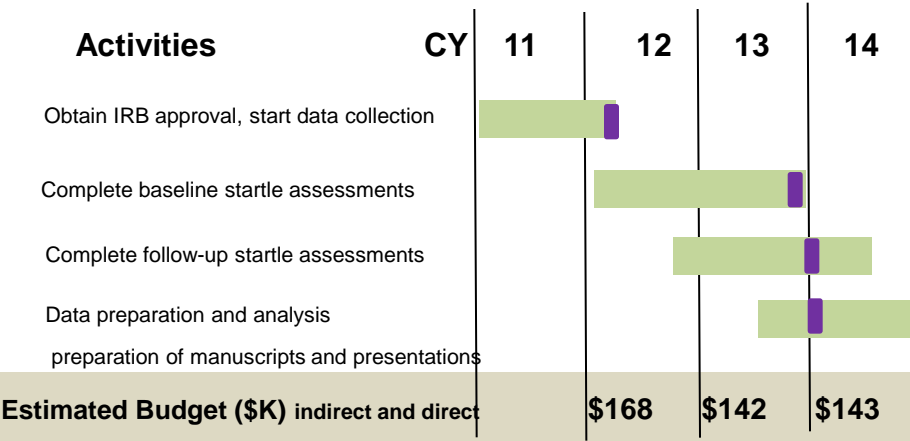
Aim 3 is exploratory and will examine whether (a) magnitude, time course and/or rate of habituation to unpleasant, neutral and pleasant pictures predicts treatment response to six-month Dialectical Behavioral Therapy (DBT) for suicidal behavior; and (b) magnitude, time course and/or habituation of affective startle improves with 6 months of DBT in treatment responders compared with non-responders.

	Baseline assessments (50% HR, 50% LR)	Randomized to treatment (HR only)	**Supplement: Startle assessments:**			
			Pt Baseline	Pt 6mo	HC Baseline	HC 6mo
Months 19-21	30	12-13	Obtain IRB approval			
Months 21-24	30	12-13	25	-----	12	----
Months 25-30	60	25	50	12 *	12	10
Months 31-36	30	5	25	25 *	6	11
Months 37-42	-----	-----	----	13 *	----	4
Months 43-48	-----	-----				

* Only 1/2 of the randomized subjects will receive DBT
** We will also need to assess 30 healthy control veterans who are not included in the funded RCT study. These healthy controls will also participate in the affective startle paradigm both at baseline and 6 month follow up. We anticipate retaining 25 of the original 30 at the six-month follow-up. We anticipate recruitment of 2 control subjects a month over 1.5 years

Accomplishment: The supplement funding was not received until **after month 24**, five months later than the original target date. However, IRB approval was accomplished rapidly by month 26 and study recruitment commenced shortly afterward. We have currently assessed **177** baseline subjects and **23** 6-month follow-up. Data analysis is complete, manuscript has been developed and currently under review for publication. Multiple presentations have occurred.

Activities	CY	11	12	13	14
Obtain IRB approval, start data collection					
Complete baseline startle assessments					
Complete follow-up startle assessments					
Data preparation and analysis					
preparation of manuscripts and presentations					
Estimated Budget ($K) indirect and direct			**$168**	**$142**	**$143**

Updated: 4/2014

Goals/Milestones

CY11 Goal – obtain IRB approval, begin recruitment and assessment of subjects for baseline startle assessment

✓ Assess 25 high risk and 12 healthy control subjects with startle paradigm by end of calendar year (*revised to 10 HR/5 LR due to 5 month delay in funding*)

CY12 Goals – ✓ complete data collection of baseline startle assessments
✓ Complete startle assessments of suicidal subjects (total n=100)
✓ Begin to obtain 6 month follow-up startle

CY13 Goal – Complete data collection of 6 month startle assessments and data analysis (we have collected 177 of 150)   ✓

Complete data collection on 6-month follow up startle assessments (collected 23 to date)

✓   **CY14 Goal-** finish startle follow-ups, prepare startle data for analysis and conduct analyses. Manuscript generation (paper submitted and under review)

☐ **Comments/Challenges/Issues/Concerns-** n/a

Budget Expenditure to date
Projected Expenditure: $452,834 total   **Actual Expenditure**: $452,759

High Risk Suicidal Behavior in Veterans - Assessment of Predictors and Efficacy of Dialectical Behavioral Therapy

DMRDP Proposal Number WX81XWH-09-1-0722

PI: Goodman, Marianne   **Org:** James J. Peters VAMC, Bronx NY   10468   **Award Amount:** $$1.279M

DMRDP

Study/Product Aim(s)

Aim 1: To examine, in a randomized controlled trial (RCT), the efficacy of a 6 month treatment with standard DBT (weekly individual sessions, skills training group and telephone coaching as needed) as compared to TAU in 120 veterans recently discharged from an acute psychiatric inpatient stay with high risk suicidal behavior. High-risk (HR) suicide subjects will undergo a comprehensive diagnostic interview prior to entering the treatment study. Subjects will receive 6 months of TAU vs. DBT but both groups will continue to receive standard psychopharmacology and case management services from their clinic providers. Subjects will receive a battery of assessments at month 6, 12 and 18.

Aim 2: To recruit veterans recently discharged from an acute psychiatric inpatient stay comparing 150 veterans with HR suicidal behavior to 150 veterans without such behavior (LR) in symptom domains focusing on interpersonal functioning and resiliency.

Aim 3: is exploratory and examines the effect of treatment (DBT or TAU) on the putative intermediate symptom domains associated with HR suicidal behavior of interpersonal functioning and resiliency.

	Baseline assessments (50% HR, 50% LR)	Randomized to treatment (HR only)	Follow-up assessments 6mo	12 mo	18mo
Months 0-6	30	15	-----	-----	-----
Months 7-12	60	25	12	-----	------
Months 13-18	60	25	19	11	-----
Months 19-24	60	25	19	17	10
Months 25-30	60	25	19	17	15
Months 31-36	30 – actual to date: **208**	5 – actual to date: **65**	19	17	15
Months 37-42	_____		3	17	15
Months 43-48	_____	_____	_____	2	15

New numbers with accepted no-cost extension:

		Treatment	follow up 6 mo	12 mo	18mo
Months 37-48 (year 4)	75	50	28	19	30
Months 49-60 (year 5)	15	5	25	50	50

Accomplishment: 384 subjects have signed consent. From this total, 340 subjects completed the baseline assessments. 93 subject have been randomized in the treatment trial which is ongoing. These data have generated 3 manuscripts (2 published, 1 under review), 8 presentations and 7 posters to date.

Activities

Activities	CY	10	11	12	13	14
Obtain IRB approval, start data collection						
Complete 300 baseline assessments						
Perform randomized clinical trial (n=120)						
Complete follow-up assessments						
Data preparation and analysis						
preparation of manuscripts and presentations						

Estimated Budget ($K) indirect and direct $318K | $339K | $353K | $376K no cost ext.

Updated: 12/2015

Goals/Milestones

✓ **CY10 Goal** – obtain IRB approval, hire and train staff, begin recruitment targeting 90 baseline assessments and 40 randomized to treatment trial. Initial DoD IRB approval was delayed 5 months behind projected date. For the remainder of 2010, we completed **55** baseline assessments and randomized **23** high risk suicidal veterans for treatment.

✓ **CY11 Goal** – continue data collection of baseline assessments (n=120) and randomization to clinical trial (n=50), and follow up assessments (n=76). Actual numbers were 96 consented subjects, **66** completed baseline assessments and **26** randomized to the tx trial.

✓ **CY12 Goal** – continue data collection of baseline assessments (n=90)   ✓ and randomization to clinical trial (n=30), and follow up assessments (n=102).

✓ **CY 13 Goal**- continue data collection of baseline assessments (n=75) and 50 subjects randomized to RTC by increasing efforts at our second recruitment site (Manhattan VAMC). Recruitment to date thru 2013- we have completed **329** baseline assessments and randomized **93** subjects to the treatment trial. Our recruitment for baseline assessments has increased due to addition of the second site, but clinical trial enrollment remains behind.

✓ **CY 14 Goal**- Complete data collection and data analysis & manuscript generation

Comments/Challenges/Issues/Concerns- recruitment for RCT as described above, addressed through addition of 5th year and no cost extension

Budget Expenditure to date Projected Expenditure:$1.279M   Actual: (through3/14) $ 1.279